REMARKS

This is response to the Final Office action (Paper No. 20070924) mailed 5 October 2007 and the Advisory action (Paper No. 20080204) dated 8 February 2008.

The response is submitted with Request for Continued Examination.

Claim 1 has been amended by this RCE Amendment.

Claims 1 through 4 and 6 through 18 are pending in this application.

Claims 8-18 were withdrawn from the examiner's consideration.

A declaration under 37 CFR 1.132 incorporating the applicant's reasoning with respect to the prior art references is submitted herewith because, in the Final Office action, the examiner disregarded the applicant's previous reasoning and arguments and made erroneous assumptions.

I. Claim Rejections – 35 USC § 103

Claims 1-3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb (EP 0230 052 A2) in view of Persselin (Clin Orthop Relat Res, 1991).

Claims 1 and 4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb EP'052 in view of Persselin and in view of L'Italien *et al.* (US 6,136,784).

Claims 1 and 6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb EP'052, in view of Persselin in view of Fletcher *et al.* (JCI, 1952) and in view of Harris (Diabetes Care, 1998).

Claims 1-3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb (US 4,710,380) in view of Gottlieb *et al.* (US 5,013,546) and in view of Persselin.

Claims 1 and 4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb'380 in view of Gottlieb *et al.*'546 in view of Persselin and in view of L'Italien *et al.*'784.

Claims 1 and 6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gottlieb'380 in view of Gottlieb *et al.*'546 in view of Persselin in view of Fletcher *et al.* and in view of Harris.

Claims 1-4 and 6-7 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8 and 13 of U.S. Patent No. 4,710,380 in view of U.S. Patent No. 5,013,546.

The examiner cites Gottlieb (EP 0230 052 A2 and U.S. Pat. No. 4,710,380) for showing the control of rheumatoid arthritis in an individual, and the examiner also cites Persselin for showing that "rheumatoid arthritis necessarily reads upon a chronic systemic inflammatory disease and that..."

The examiner also argued that "the origin of the chronic inflammation is not specified, thus, the claims read upon treating any type of chronic inflammation in an individual having Metabolic Syndrome."

Claim 1 has been amended to recite "chronic inflammation associated with Metabolic Syndrome in an individual having the Metabolic Syndrome".

First, the examiner failed to show that all the claim limitations were taught or suggested by the prior art.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

Here, the inventor of Gottlieb (EP 0230 052 A2 and U.S. Pat. Nos. 4,710,380 and 5,013,546) was the husband and professional colleague of the inventor of the present invention. Dr. A. Arthur Gottlieb (EP 0230 052 A2) mentions diabetes, and Gottlieb U.S. Pat. Nos. 4,710,380 mentions Type I diabetes. Even if Gottlieb (EP 0230 052 A2) does not specifically state that the diabetes is Type I diabetes, the diabetes in Gottlieb (EP 0230 052 A2) is Type I diabetes. Where diabetes is mentioned in Gottlieb (EP 0230 052 A2), it is mentioned in a list with rheumatoid arthritis, because it is an autoimmune disease and not because of any other relationship between the two. This is evidenced by other Gottlieb's patents such as U.S. Pat. Nos. 4,710,380 and 4,920,097. The examiner is taking the reference to diabetes out of proper context. The World Health Organization recognizes three main forms of diabetes: type I, type II, and gestational diabetes (occurring during pregnancy), which have some similar signs, symptoms, and consequences, but different causes and population distributions. Type I diabetes is an autoimmune disease which results in the destruction of Beta cells of the Islets of Langerhans which are located in the pancreas. The Beta cells produce insulin. Hence, their destruction results in a lack of insulin and the inability of the body to use glucose. That glucose then accumulates in the blood, resulting in elevated glucose. The elevated blood glucose of Type I diabetes is a result of hypoinsulinemia. Such individuals are typically underweight. There is no

obesity associated with Type I diabetes, as there is in Type II diabetes and in the Metabolic Syndrome.

The examiner's reference to Persselin is also not proper. While Persselin's paper does refer to rheumatoid arthritis as a chronic inflammatory disease, he appears to be dealing with this disease strictly from a clinical point of view. The cause of Rheumatoid Arthritis is an autoimmune reaction in which the joints are attacked by the patient's own immune system, resulting in damage to the joints. Such destruction subsequently results in chronic inflammation from rubbing of unprotected bone. Gottlieb, in his earlier patents discusses treatment of the autoimmune reaction, NOT the subsequent inflammation. Neither Gottlieb nor Persselin discuss a relationship or association between rheumatoid arthritis and the Metabolic Syndrome.

Claims 1-4, 6 and 7 of the present application are directed to the control of chronic inflammation associated with Metabolic syndrome. The present invention teaches that since chronic antigenic stimulation resulting from immune dysfunction leads to the inflammatory condition which is characteristic of the Metabolic Syndrome, then correction of immune dysfunction can reduce the symptoms and characteristics of the Metabolic Syndrome, and thus the factors leading to Metabolic Syndrome related diabetes mellitus and coronary heart disease. Persselin does not disclose that the cause of rheumatoid arthritis is associated with Metabolic Syndrome. As stated above, the autoimmune reaction of Rheumatoid Arthritis, results in a decrease of joint cartilage and inflammation secondary to the joint bones rubbing against each other, without protection normally provided by the cartilage. What is important for the examiner to understand is that inflammation may be caused by many things.

That is, Gottlieb, Persselin, or combination thereof did not teach in any way the treatment of chronic inflammation in an individual having Metabolic Syndrome (i.e., chronic inflammation associated with Metabolic syndrome) as claimed in the present application.

Second, please also note that the Metabolic Syndrome is a complex constellation of symptoms and conditions which tend to appear in a cluster. That it is different than other conditions has been recognized by the world medical establishment and it has been assigned its own ICD Code (International Classification of Disease), 277.7, whereas the code for Diabetes Mellitus is 250 followed by a decimal point and number specifying the different "varieties" and status of the disease. Treatment of the Metabolic Syndrome is complex and depends on what parts of the constellation of conditions are present in any given individual. The Metabolic Syndrome is not equivalent to any type of Diabetes Mellitus or obesity, although impaired glucose tolerance and obesity may well be components of the Metabolic Syndrome as it is expressed in a given individual. It must also be said that, because there is variability in the expression of the Metabolic Syndrome, other than for inflammation, there is no universal treatment that has been found to treat it. Further, it must also be said that, although members of the medical establishment has have tried, no clear treatment of the Syndrome has been found to be "obvious".

The instant application addresses an area of commonality which was discovered by extensive research into the various components of the Metabolic Syndrome and a sophisticated re-analysis of an experimental study in which immunomodulatory therapy indicated success.

It is important that the examiner recognize that just because Rheumatoid Arthritis has an inflammatory component, it is not the same as the Metabolic Syndrome. Further, the earlier

Gottlieb patents addressed the treatment of autoimmune diseases such as Rheumatoid Arthritis and Type I Diabetes Mellitus, which is clearly not the type of Diabetes found in the Metabolic Syndrome. (As well, Rheumatoid Arthritis and Type I Diabetes do not lead, as a result of the course of disease, to obesity.) Further, Dr. A. Gottlieb taught in his patents that the use of the technology described in the instant application affects autoimmune diseases as well as diseases involving immune deficiency. A careful search of Gottlieb's patents reveals that he did not teach in any way that the technology of the instant application would treat chronic inflammation. We point out again that the parenthetical list of autoimmune diseases in Dr. A. Gottlieb's patents that includes Rheumatoid Arthritis and Diabetes is a list of autoimmune diseases.

The examiner states that her search was broadened to include "impaired glucose tolerance associated with the Metabolic Syndrome." The examiner then goes on to associate Diabetes and obesity with Gottlieb's teachings about Diabetes in prior patents, saying that impaired glucose tolerance is associated with Diabetes. There are numerous conditions and reasons for impaired glucose tolerance, including Type I Diabetes which is the subject of Gottlieb's statements in prior patents. (Note that the term "Diabetes Mellitus", a term that dates to antiquity, simply refers to "sweet urine", a symptom of any number of conditions, some related only by that symptom.) The Examiner then states that giving of insulin can result in obesity and through some contorted logic, links all of the conditions and declares that what we claim (in the claims that she has not insisted be disallowed) is obvious or is present in other patents. The examiner simply is not allowed to make all of the "logical" jumps she makes, as they are not supported by the science. Further, the use of an immunomodulator to control a metabolic disease is certainly new, unique, and not obvious to anyone. Rather, it grew out of a sophisticated analysis of data collected and examined by Gottlieb and his colleagues.

The examiner improperly equated Rheumatoid Arthritis with the glucose intolerance and/or Diabetes associated with the Metabolic Syndrome. If Rheumatoid Arthritis is an autoimmune disease, then it does, as we state, fall into a similar category of diseases as Type I Diabetes Mellitus. This is the relationship discussed by Gottlieb in the prior patents cited by the examiner.

The Examiner has taken words from various sources and made improper assumptions of identity. Diabetes mellitus can be Type I Diabetes mellitus, Type II Diabetes mellitus, or Diabetes mellitus associated with the Metabolic Syndrome. To be specific:

Type I Diabetes Mellitus: an autoimmune disease which prevents production of insulin by cells of the pancreatic islets of Langerhans. It is a genetic disease with a recessive pattern of inheritance (Gottlieb, M.S and Root, H.F. Diabetes Mellitus in Twins. *Journal of the American Diabetes Association*, 17:693-704 (1968).) Type II Diabetes Mellitus is a genetic disorder with a dominant pattern of inheritance which involves failure of the end organ (for example, muscle and liver) to use insulin.

"Type II Diabetes Mellitus" associated with the Metabolic Syndrome is a general inflammatory response causing failure of the end organs to use insulin. This form of Diabetes Mellitus is not genetically inherited.

Next, the word obesity may be that associated with excess insulin or that associated with the metabolic syndrome, among other conditions, none of which are identical in cause or treatment. Taking words out of context to find reasons for rejection does not contribute to progress.

It should be also noted that we assume that both the Diabetes included by Gottlieb and the Diabetes of the Metabolic Syndrome both result in elevated blood glucose, the reason and the

treatments are not the same. Further simply giving more insulin to a person with Metabolic Syndrome, as one might do to regulate the Diabetes included by Gottlieb, would not be expected by itself to reduce blood glucose, as the end-organs which require glucose would not be able to use that insulin.

Further, just because obesity may be associated with certain non-metabolic syndrome Diabetes therapy does not mean that it is caused by the same mechanism.

The equalities that the examiner is trying to draw simply are not valid. For example, obesity can have many root causes, as can elevated blood sugar, as can chronic irritation. To form equalities across all of these is incorrect. To do so would be the same as to say that there is only one way to treat a person who is sneezing, where sneezing can be caused by a cold (viral) or, for example, by exposure to dust (a physical irritation), or by an allergic reaction. In the first case, there is no good treatment, in the second, one would put on a mask, and in the third, one would take an antihistamine. In no case would one treatment be expected to provide relief in place of the other. In the same way, no one skilled in the art would presume that Diabetes listed with Rheumatoid Arthritis and/or other autoimmune diseases would be other than Type I Diabetes. Additionally, no one skilled in the art would presume that Type I Diabetes and the impaired glucose tolerance or Diabetes of the Metabolic Syndrome are the same condition or that they would be treated in the same way. Anyone trying to treat a person with the Metabolic Syndrome in the same way as one would treat a person with Type I Diabetes would be making a serious error. The ordinary skilled person in the art would not make such presumptions.

For the foregoing reasons, claims 1 through 4, 6 and 7 are patentable.

In view of the above, all claims are deemed to be allowable and this application is believed to be in condition to be passed to issue. Reconsideration of the rejections and objections is requested. Should any questions remain unresolved, the Examiner is requested to telephone Applicant's attorney.

A fee of $635.00 is incurred for **SMALL ENTITY** by the submission of the Request for Continued Examination (RCE) ($405.00) and two-month extension of time ($230.00). Should the other fees be incurred, the Commissioner is authorized to charge Deposit Account No. 02-4943 of Applicant's undersigned attorney in the amount of such fees.

Respectfully submitted,

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